REMARKS

The Examiner makes the following rejections:

A. Claims 50, 99, 100, and 108 are rejected as allegedly obvious under section 103(a)[1] on the basis of Walt, in view of Felder, Chang, or Ravkin, when taken with Peters.

B. Claims 50, 99, 100, and 108 are rejected as allegedly obvious under section 103(a) on the basis of Walt, in view of Felder, Chang, or Ravkin, when taken with Kaetsu.

C. Claims 50, 76, 99-100, 108-109, 111, 113, 119 and 120 are rejected as allegedly obvious under section 103(a) on the basis of Walt, in view of Felder, Chang, or Ravkin, when taken with Pope, Dakss and Peters.

D. Claims 50, 76, 99-101, 103-105, 108-111, 113-115, 119 and 120 are rejected as allegedly obvious under section 103(a) on the basis of Walt, in view of Felder, Chang, or Ravkin, when taken with Pope, Dakss and Kaetsu.

E. Claims 103 is rejected as allegedly obvious under section 103(a) on the basis of Walt, in view of Felder, Chang, or Ravkin, when taken with Pope, Dakss, Kaetsu and Wang.

Applicants traverse and offer the following response.

A. The New Declaration Removes Chang and the Ravkin Publication

Applicants previously submitted a Rule 131 Declaration swearing behind the December 1, 2000 filing date of Chang et al. and November 2003 date of Ravkin. The Examiner argued that the Declaration was deficient. Applicants disagree. Nonetheless, to further the prosecution, Applicants submit a new 131 Declaration signed by all of the inventors indicating the invention was conceived and reduced to practice in the U.S. The evidence provided shows a submission date of September 2000 and the Examiner can take note of the February 2001 filing date; filing a patent application within five months

[1] The Office Action indicates section 102(e) – and yet the rejections come after citation to section 103. Therefore, applicants assume an obviousness rejection was intended.

of an invention disclosure is *prima facie* evidence of diligence. The filing amounts to a constructive reduction to practice. Moreover, the Examiner can take note of the experiments set forth in the provisional for evidence of an actual reduction to practice. The declaration sets forth the dates for when the disclosure was diligently submitted to the licensing office, as well as the date of filing. These are factual statements showing the timing involved. In view of this, it is respectfully submitted that the Declaration is sufficient to remove Chang and the 2003 publication of Ravkin as prior art.

B. Walt Fails To Disclose Elements And Teaches Away

1. Walt Does Not Teach A Plurality Of Different Geometric Shapes

The Examiner uses the Walt patent as the primary reference in every rejection. The Examiner argues that Walt teaches non-spherical shapes. Applicants respectfully submit that Walt teaches spheres – and in one line teaches "irregular" shapes. Walt is silent about the use of any defined shape other than spheres, i.e. there is no teaching of a plurality of different geometric shapes. Importantly, there is no teaching of using different defined shapes as a basis for determining analyte binding (in fact, it is not clear how this could be done with "irregular" shapes).

2. Walt Does Not Teach A Sensor Having First And Second Portions of Different Shape

Claim 76 specifies "wherein the shape of the first portion of the sensing elements is different from the shape of the second portion of the sensing elements." Walt does not teach anything relevant in this regard. Indeed, the Examiner appears to overlook this limitation in Claim 76.

3. Walt Does Not Teach Curing To Impart A Shape

The Examiner cites to col. 17, lines 47 – col. line 2 for the proposition that Walt teaches "curing the liquid composition to form a supporting member" (Office Action, p.10). First, the term "cure" or "curing" does not appear in that portion (or any portion) or the Walt patent. Second, the curing is not done to impart a shape to the sensor (see Claims 119 and 120), let alone a geometic shape. Third, the cited section teaches only evaporation of the solvent – not light curing (see new Claims 121 and 122). Fourth, the use of the Nafion polymer is to hold the beads in the wells ("Upon solvent evaporation, a

thin film of Nafion was formed over the microspheres which holds them in place."). Thus, even if the Nafion can be said to have been "cured" (which Applicants do not concede), the cured material does not have a different shape (see Claim 50), let alone first and second portions of different shape (see Claim 76).

4. Walt Teaches Discrete Sites For Determining Location

Applicants' specification discusses prior art array approaches that focus on the location (or address) of the signal:

> "All of these [prior art] systems require the placement of the receptors at predetermined locations. The presence or absence of an analyte may be discerned by monitoring a specific location of a sensor array of receptors."

(see specification at p. 5). Applicants' specification goes on to distinguish the approach of the present invention:

> "Thus, the presence of a particular analyte may be determined by the observance of a signal from a sensing element having a predetermined shape and/or size. This offers an advantage over conventional systems, where the shape and/or size of the particle, **rather than the location** of the particle, determines the identity of the analyte."

(see specification at p. 6, emphasis added) Walt, however, indicates that location is "key" by emphasizing attachment at "discrete sites":

> "It should be noted that a key component of the invention is the use of a substrate/bead pairing that allows the association or attachment of the beads at discrete sites on the surface of the substrate, such that the beads do not move during the course of the assay."

Even where the beads are randomly placed on the "patterned" surface, Walt indicates the "decoding" involves determining the location:

> ". . . the bioactive agents may be synthesized on the beads, and then the beads are randomly distributed on a patterned surface. Since the beads are first coded with an optical signature, this means that the array can later be "decoded", i.e. after the array is made, a correlation of the location of an individual site on the array with the bead or bioactive agent at that particular site can be made."

This amounts to a teaching away, since Applicants claim detection of analytes based on sensor shape – not location.[2] The Examiner is reminded that a "reference may be said to teach away when a person of ordinary skill, upon [examining] (sic) the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *Para-Ordnance Manufacturing v. SGS Importers International*, 37 USPQ2d 1237,1241 (Fed. Cir. 1995) (quoting *In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994)). It is respectfully submitted that one of skill in the art would be led by Walt to take the path of associating signal with location – not with shape.

C. Felder Also Lacks Elements And Teaches Away

1. Felder Does Not Teach A Plurality Of Different Geometric Shapes

The Examiner combines Felder with Walt in every rejection. The Examiner argues that Felder teaches different shapes. Applicants respectfully submit that Felder provides no specifics regarding shapes. Felder is silent about the use of any defined shape, i.e. there is no teaching of a plurality of different geometric shapes.

2. Felder Does Not Teach A Sensor Having First And Second Portions of Different Shape

Claim 76 specifies "wherein the shape of the first portion of the sensing elements is different from the shape of the second portion of the sensing elements." Felder does not teach anything relevant in this regard. Indeed, the Examiner appears to overlook this limitation in Claim 76.

3. Felder Emphasizes Location And Teaches Away

The Felder patent also emphasizes location by requiring "spatially discrete regions," and therefore also teaches away from the Applicants' direction:

> "This combination comprises a surface comprising a plurality of spatially discrete regions, which can be termed test regions and which can be wells, at least two of which are substantially identical. Each surface comprises at least two, preferably at least twenty or more, e.g., at least about 25, 50, 96, 864, or 1536, etc., of such

[2] Amendments to Claims 50 and 76 have been made to further the prosecution, without acquiescing to the rejection. Applicants hereby reserve the right to prosecute the unamended (or similar) claims in the future.

> substantially identical regions. Each test region defines a space for the introduction of a sample containing (or potentially containing) one or more targets and contains a biological or chemical array.

(See Felder, Summary of the Invention). Indeed, Felder teaches that one must have at least two identical discrete regions (see above quote). Felder indicates that standard 96-well plates (or plates with more wells) can be used. As the Examiner is probably aware, standard 96-well plates provide an address for each location based on a letter/number combination which corresponds to the row and column of the well. Felder emphasizes that, regardless of the system used: "The surface comprises regions which are spatially discrete and addressable or identifiable." This is in contrast to Applicants' claimed embodiment, which utilizes shape rather than location. One skilled in the art would be led by Felder to employ spatially discrete regions (as shown in the many drawings) to identify the analyte. Indeed, Felder teaches the use of a "Key" to the pattern based on location: "different oligonucleotide anchors were dispensed within each well in the pattern shown as the Key (left side of the figure)." (see Felder, Example 1).

D. Wang Teaches Away

The Examiner cites the Wang patent as evidence for employing "any known shape." (Office Action, p.13). Applicants cannot agree. A careful reading of Wang indicates that the shape is not used to determine analyte binding. Rather, the shape is used to secure the particle to the substrate:

> "For greater stability the pits in the substrate and the particles as depicted in FIG. 2E may have a variety of shapes, such as a particle with a pyramidal shape 52, cubic shape 54, or conical shape 56. In this way, once the particle has become accommodated in the indent or pit in the substrate, it will be held firmly in position. Of course, the various shapes may be used with other modes for orienting the particles, such as the vacuum orientation. In addition, different shapes may be employed to orient particles to different sites, so that shapes and sizes may be used to provide sections or segments of different particles with different bound components."

Thus, Wang adds nothing. Indeed, it also focuses on location by using "spokes" as convenient ways to organize the array into "sectors":

> "In FIG. 3A, disk 58 has linear radial arrays 60 of particles, where each spoke 62 may be the same particles or different particles, where each spoke may have a header to define the nature of the particles in the specific spoke and each spoke 62 is added individually. FIG. 3B is analogous to 3A, except that on disk 58b, particles 60b are added in a pattern, so that a plurality of spokes 62b are formed contemporaneously, where the particles 60b in any one position in the pattern of spokes 62b are the same composition, so as to result in sectors having the same organization of compositions. Each of the disks has a central orifice 64 for mounting on a spindle for circular movement. Instead of radial placement of particles and headers, in FIG. 4, disk 66 has a plurality of circular grooves, exemplified by a single groove 68, in which particles 70 are evenly circularly placed. Each groove may have particles having the same or different composition, where for each different composition a different header may be employed in the groove or a different particle, which provides for coding to identify the associated particles."

Thus, one of skilled in the art would be led by Wang to define "sectors" on the array and associate them with the nature of the compositions – rather than associate the compositions with a unique shape. In sum, Wang teaches away.

E. Non-Analogous Art

a. Peters Teaches "Dip Sticks" – not a plurality of different receptors on sensors of different shapes

Peters does not remedy the defects of Walt, Felder and Wang. Indeed, Peters is non-analogous art in that it seeks to improve "dip sticks" and "test strips" – not assays that permit multiple analytes to be assayed simultaneously. Dip sticks and test strips are typically used for single analytes (e.g. to detect a hormone indicative of pregnancy in the urine – see the Examples in the Peters spec). Moreover, Peters uses polymer to impregnate a solid support – not to create sensors of different shapes.

b. Dakss and Pope Teach Light-Curing Of Adhesives

Dakss and Pope are directed to the attachment of microspheres to optical fibers with a light-cured adhesive. Applicants submit this is non-analogous art. The Examiner argues that Dakss is relevant in the context of Walt and Pope and argues that Applicants previous response was "completely silent" regarding Walt and Pope. (Office Action, p.23). This is not accurate. The previous response pointed out that Walt did not anticipate the claims – and the anticipation rejection was withdrawn! Walt was therefore discussed. With respect to Pope, Applicants previous response noted: "Applicants have highlighted the deficiencies in Dakss (and pointed out that Pope, Peters and Kaetsu do not remedy these deficiencies)." (see prior Response, p. 9). Therefore, Pope was discussed in the context of the deficiencies in Dakss. Moreover, while Walt, Pope and Dakss all relate to optical fibers – optical fibers have NO relevancy to the pending claims. Pope and Dakss are seeking to solve a problem that is not pertinent to the problem solved by the claimed embodiment.

The problem Applicants seek to solve is to allow detection of analytes without being confined to using receptors attached to fix positions in one large ordered array; rather, by using a plurality of smaller sensors of different shapes, one can use random arrays. Thus, the Dakss and Pope references have a different purpose.

Without waiving the non-analogous art argument, Applicants submit that even if these references are combined with Walt, Felder and Wang, the combination does not teach all the elements set forth in the pending claims. Specifically, Dakss and Pope appear to be cited by the Examiner only to show that light-cured adhesives are known. This adds nothing. As noted above, the claim language requires that the "cured material" have different shapes (see Claim 50). Dakss and Pope do not provide this teaching. Walt does not provide this teaching. Felder does not provide this teaching. Wang does not provide this teaching. Peters does not provide this teaching (as noted above, Peters uses a polymer in the context of a solid support, such as a bead to "impregnate" the solid support – thus, different shapes are not achieved with the polymer). Kaetsu also does not provide this teaching (Kaetsu is focused on keeping enzyme activity in order to be able to re-use the enzyme – and says nothing about shape).

Applicants stress that EVERY reference cited and combined by the Examiner have been addressed above, and yet elements of the pending claims are missing. As such, the obviousness rejection cannot stand.

F. The *Keller* and *Merck* Cases Are Inapplicable

The Examiner – once again - cites the *In re Keller* and *In re Merck & Co.* cases to support the legal proposition that one cannot attack the references individually. This is not correct. These cases apply to the situation where only one reference is rebutted and where the applicant remains silent on the other references in the combination. This is not the case here. Applicants have provided an argument regarding the primary reference (Walt) and each of the other references (Felder, Chang, Ravkin, Pope, Dakss, Peters, Kaetsu and Wang). Applicants have highlighted the deficiencies in Dakss (and pointed out that Pope, Peters and Kaetsu do not remedy these deficiencies). Thus, there is no basis for the position that Applicants have ignored other references in the combination.

CONCLUSION

It is believed that the arguments and amendments (as well as the 131 Declaration which removes certain references as prior art) render the claims allowable. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicants encourage the Examiner to call the undersigned collect at (781) 828-9870.

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By: _____
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